DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/08/2010 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 11/08/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 11/10/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 11/08/2010, claims 1, 3, 4, 33, 39 and 87-90 are under examination and claims 19, 21-22, 27, 34-36, 40-63 and 91-108 are withdrawn from further consideration as being drawn to a non-elected invention.

Response to Arguments

Claim Rejections - 35 USC § 112

The rejection of claims 1, 3, 4, 33, 39 and 84-90 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter) is withdrawn.

The rejected claims 1, 3-4, 33, 39 and 84-90 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement that was previously maintained is now withdrawn.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 3, 4, 33, 39 and 87-90 under 35 U.S.C. 103(a) as being unpatentable over McSwiggen et al. (US 2004/0192626 of record) is maintained for the reasons of record.

Applicant's arguments filed 11/08/2010 have been fully considered but they are not persuasive. Applicant argues McSwiggen et al. do not disclose siRNA molecules wherein the antisense strand and the sense strand comprise 2'-fluoro pyrimidine nucleotides and the antisense strand further comprise 2'-deoxy purine but acknowledges that McSwiggen et al. do teach siRNA molecules wherein both strands comprise 2'-fluoro pyrimidine nucleotides and 2'-deoxy purine.

This argument is not convincing because the sense strand of the instantly claimed siRNA is not limited such that the sense strand does not contain 2'-deoxy

nucleotides. The claims recite the sense strand comprise uridines, cytidines, adenosines and guanosines but does not limit the purines to a specific type. Thus the sense strand can comprise 2'-deoxy purines.

McSwiggen et al. exemplifies a siRNA wherein the pyrimidines are substituted with 2'- fluoro groups and the purines are substituted with 2'-deoxy groups on both the sense and antisense strands wherein a 2'-deoxy adenosine or guanine is located at nucleotides 6-10 and 17-21 from the 5' end of the antisense strand which would meet the limitations of the instant claims as explained above (see Figures 18F and 19F). Moreover, McSwiggen et al. teach the sense strand can be modified with 2' fluoro nucleotides only and further teach the antisense and/or the sense strand can comprise combinations of modified nucleotides such as 2' fluoro groups as well as 2'-deoxy groups and teach specific embodiments wherein the antisense strand comprises pyrimidine nucleotides modified with a 2'-fluoro and purine nucleotides modified with 2'-deoxy groups (see at least paragraphs 0026, 0027, 0057 and 0107). The modified siRNA taught by McSwiggen et al. has priority in WO 03/074654, Figures 18 and 19.

At paragraph [0011-0012], McSwiggen et al. teach the introduction of chemically modified nucleotides provide a powerful means to overcome the limitations of in vivo stability and bioavailability inherent to native RNA molecules and teach the modified siRNA molecules have increased stability but are able to still mediate RNAi (see paragraph 0111). McSwiggen et al. teach the siRNA molecule has a cleavage site for RISC which mediates cleavage of the target gene (see paragraph 0005) and references

the work of Elbashir et al. (Genes and Dev 2001 also cited on IDS filed 02/27/2006) which identifies the cleavage region of siRNA.

McSwiggen et al. do not specifically teach the siRNA comprising modified nucleotides retains the ability to inhibit expression of the target mRNA by at least 30% however beginning at paragraph [0315] McSwiggen et al. teach optimizing the activity of the siRNA comprising modified nucleotides to preserve the ability of the siRNA to mediate RNAi efficiently in cells. It would have been obvious to one of ordinary skill in the art to synthesize a siRNA comprising chemically modified nucleotides as taught above and optimize the incorporation of said modifications to obtain a siRNA with the highest ability to inhibit the desired gene expression.

Beginning in Example 1, McSwiggen et al. teach detailed steps on constructing the said siRNA molecules and methods of testing the activity of said siRNA against the target gene. Given that McSwiggen et al. teach the introduction of chemically modified nucleotides provides a powerful means to overcome the limitations of in vivo stability and bioavailability inherent to native RNA molecules, one would have clearly incorporated said modifications into a siRNA and would have optimized the position and number of modified nucleotides to obtain a siRNA with the highest ability to inhibit the desired gene expression. Moreover, given that there are a multitude of general methods and strategies to determine the location of incorporation of chemically modified nucleotides as taught by McSwiggen et al., one of ordinary skill in the art would have expected to be able to determine the location of incorporation of chemically modified

nucleotides as instantly claimed while maintaining the siRNAs ability to inhibit gene expression by at least 30%.

Thus, the invention as a whole would have been prima facie obvious to one of skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact the SPE for 1635 Heather Calamita at 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1635